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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,140	10/06/2003	Weiniu Gan	CL001165DIV	1062

25748 7590 04/21/2006

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EXAMINER	
TIDWELL, JUDY LILLE	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/678,140	GAN ET AL.	
	Examiner	Art Unit	
	Judy Lille Tidwell, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/14/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 24-38* is/are pending in the application.

4a) Of the above claim(s) *1,2,37 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 24-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibit A*.

Gan et al.

DETAILED ACTION

Election/Restrictions

The Election filed on 03/14/2006 in response to the Restriction Requirement of 02/14/2006 has been entered. Applicant's election of Group II, claim 3 drawn to an isolated antibody that selectively binds to a polypeptide, wherein the amino acid sequence of said polypeptide consists of SEQ ID NO: 2, has been acknowledged.

Claims 1-3, 24-38 are currently pending. Claims 1,2, 37-38 are withdrawn from consideration as being drawn to non-elected inventions. Claims 3, 24-36 are examined on the merits.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3, 24-36 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial utility, a credible asserted utility, or a well-established utility.

Claims 3, 24-36 are interpreted as drawn to an isolated antibody that selectively binds to a polypeptide, wherein the amino acid sequence of said polypeptide consists of/comprises SEQ ID NO: 2. The specification speculates that SEQ ID NO:2 might have potential utilities, based primarily on the source of the protein as well as the class/action of the protein (page 18) as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins, and serve as targets for the development of human therapeutic agents that modulate Ras-like protein activity in cells and tissues that express the Ras-like protein (page 6), used for the development of commercially important products and services (page 8), biological assays, drug screening assays, identification of compounds that modulate Ras-like protein activity, treatment of a disorder (page 19-20), competition binding assays (page 23), two- or

three-hybrid assay (page 24), diagnostic assay (page 26), *in vitro and in vivo* techniques for detection of peptides (page 26-27), pharmacogenomic analyses (page 27), in making antibodies coupled to a detectable substance (page 28-29), and the uses of the antibody thereof including protein isolation, immunohistochemistry, protein expression, subcellular localization, pharmacogenomic analyses, tissue typing, inhibiting protein function, and the creation of kits for using antibodies to detect the presence of a protein in a biological sample (page 29-31). These utilities are not considered to be specific and substantial because neither the specification nor any art of record teaches what the biological activities of SEQ ID NO:2 are, how they function, or a specific and well-established utility for SEQ ID NO:2 protein or antibody.

Although the specification (page 1-8) speculates the possibility that SEQ ID NO:2 is a Ras-like protein, a kinase, based on homology, the specification fails to teach what kind(s) enzymatic reaction the protein carries out.

Voet et al. (1990, Biochemistry, John Wiley & Sons, page 429) teach that there are numerous kinases, each working on a specific substrate and generating a specific product, for example hexokinase uses glucose as its substrate to produce glucose-6-phosphate while phosphofructokinase uses a different substrate and produces a different product: this indicates that the different kinases carry out distinctly different enzymatic reactions although these kinases belong to the same family having a common structural domain and sequence homology. The instant specification does not disclose the nature of the substrate the instant SEQ ID NO: 2 works on.

Further, the art generally acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. Scott et al (Nature Genetics, 1999, 21:440-443) teach that the function of newly identified gene products is unpredictable even when the database searches reveal significant homology to proteins of known function. Scott et al teaches that the gene causing Pendred syndrome encodes a putative transmembrane protein designated pendrin. Based on sequence similarity data, the authors postulated that the putative protein was deemed to be a member of sulfate transport proteins that included a 29% identity to rat sulfate-anion transporter, 32% similarity to human diastrophic dysplasia sulfate transporter, and

45% similarity to the human sulfate transporter 'downregulated in adenoma'. However, upon analyzing the expression and kinetics of the protein, the data revealed no evidence of sulfate transport wherein results revealed that pendrin functioned as a transporter of chloride and iodide. Scott et al. states that these results underscore the importance of confirming the function of newly identified gene products even when the database searches reveal significant homology to proteins of known function (page 411, 1st column, 4th paragraph).

Skolnick et al. (2000, Trends in Biotech. 18:34-39) also states that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Finally, Bowie et al. (1990, Science 247:1306-1310) state that determination of three dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (p. 1306). Thus, the specification fails to support the asserted credible, specific and substantial utility of the newly identified instantly claimed protein.

Furthermore, the specification does not teach a relationship to any specific disease or establish any involvement of SEQ ID NO:2 protein in the etiology of any specific disease. The specification does not teach a relationship between the different tissue distribution of the cDNA SEQ ID NO:1 (page 7, Figure 1) to any specific disease or etiology of any specific disease, either. None of the disorders listed from page 20 through page 21 is caused by the differential distribution of neither SEQ ID NO:1 nor SEQ ID NO:2. The tissue distribution of the cDNA SEQ ID NO:1 (page 7, Figure 1) does not lead to diagnosis any of the disorders. None of the disorders listed from page 20-21 is caused by the malfunction of the protein. The specification does not have any credible use for the antibodies, either. Making and purifying the protein or antibody encoded by SEQ ID NO:2 and the various assays recited in the instant application do not lead to substantial and credible uses of the claimed invention due to unknown functions of the protein encoded by the claimed invention. Nothing is specific to the sequences of the claimed invention for all of the various uses. The specification does not have any credible use for pharmaceutical compositions, predictive medicine, diagnostic assay, prognostic assays, monitoring effects during clinical trials, and methods of treatment because the specification does not teach what disease(s) is caused by malfunction of the claimed invention or the protein encoded by it. Since SEQ ID NO:2 does not have specific and substantial utility, a credible asserted utility, or a well-established utility, a compound that binds to SEQ ID NO:2 does not have specific and substantial utility, a credible asserted utility, or a well-established utility.

After further research, a specific and substantial credible utility might be found for the claimed invention. This further characterization, however, is part of the act of invention and until it has been undertaken, applicant's claimed invention is not

complete. Therefore it is concluded that the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention without undue experimentation.

In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an **immediately obvious or fully disclosed "real world" utility**. The instant claims are drawn to antibody to SEQ ID NO: 2 which has undetermined function or biological significance. Until some actual and specific activity can be attributed to the protein identified in the specification as SEQ ID NO: 2 or the polynucleotides encoding it, the claimed invention is incomplete.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 24-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Hayward et al. (WO-98/53061-A1, published 11/26/1998).

Claim 3 is drawn to an isolated antibody that selectively binds to a polypeptide, wherein the amino acid sequence of said polypeptide consists of SEQ ID NO: 2. Claim 24 is drawn to an isolated antibody that selectively binds to a polypeptide, wherein the amino acid sequence of said polypeptide comprises SEQ ID NO: 2. Claim 25 further limits claim 3, and claim 26 further limits claim 24, wherein the antibody of the

respective base claim is a monoclonal antibody. Claim 27 is drawn to claim 3, claim 28 is drawn to claim 24, claim 29 is drawn to claim 25, and claim 30 is drawn to claim 26, wherein the antibody is coupled to a detectable substance. Claim 31 is drawn to claim 3, claim 32 is drawn to claim 24, claim 33 is drawn to claim 25, and claim 34 is drawn to claim 26, a composition comprising an antibody and a pharmaceutically acceptable carrier. Claim 35 is drawn to an isolated antibody fragment that selectively binds to a polypeptide, wherein the amino acid sequence of said polypeptide consists of SEQ ID NO: 2, and wherein the antibody fragment comprises a fragment selected from the group consisting of: an Fab fragment, an $F(ab')_2$ fragment, and an Fv fragment. Claim 36 is drawn to an isolated antibody fragment that selectively binds to a polypeptide, wherein the amino acid sequence of said polypeptide comprises SEQ ID NO: 2, and wherein the antibody fragment comprises a fragment selected from the group consisting of: an Fab fragment, an $F(ab')_2$ fragment, and an Fv fragment.

In the instant specification as originally filed, paragraph #0103 (also page 28) reasonably communicates that the limitation "selectively binds" means that the antibody not only binds to a polypeptide consisting of SEQ ID NO: 2, but also binds to a polypeptide with some degree of variance. Hayward et al. in WO-98/53061-A1 (page 70, SEQ ID NO: 7) teach an antibody that binds to a polypeptide that has 98.9% homology to the instant SEQ ID NO: 2 (see attached Exhibit A). Hayward et al. also teach a monoclonal or polyclonal antibody or fragments of antibodies such as Fab fragments (page 23, lines 27-28). Furthermore, Hayward et al. teach the antibody coupled to fluorescent compounds (page 27, lines 19-20) and a pharmaceutically acceptable carrier (page 28, lines 277-29).

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Judy Lille Tidwell, PhD whose telephone number is 571-272-5952. The examiner can normally be reached on 8:00AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JLT
Art Unit 1642

MISOOK YU
PRIMARY EXAMINER